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(54) **Xylobiose containing composition.**

(57) Xylobiose-containing skin preparations for external use are disclosed. Skin preparations for external use into which xylobiose may be incorporated include cosmetics such as clear lotions, milky lotions, packs and lip treatments, drugs or quasidugs such as ointments and cataplasms, hair-care products such as rinses and hair conditions, and detergents such as hair shampoos and body shampoos. Xylobiose is typically contained in an amount of 0.0001 - 20 wt%, preferably 0.1 - 10 wt%, of the total amount of the skin preparation on a dry solids basis. The incorporation of xylobiose is effective not only in preventing the occurrence of stickiness, color change and malodor in the skin preparations but also in providing enhanced moisture retention and reducing excessive roughness and dryness of the skin and hair.

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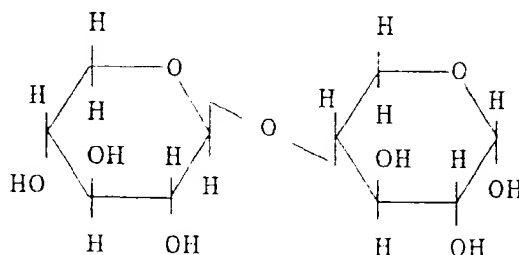
This invention relates to skin preparations for external use that are effective not only in reducing excessive roughness and dryness of the skin to impart a natural moistness and luster but also in reducing excessive roughness and dryness of the hair to give a natural oiliness.

One of the major objectives of applying cosmetics and other skin preparations for external use is to prevent and reduce excessive roughness and dryness of the skin. To this end, various humectants have been incorporated in skin preparations for external use. However, conventionally used humectants have their own problems. For example, polysaccharides tend to cause precipitation when used in alcoholic formulation; polyhydric alcohols and chondroitin sulfate cause stickiness or a slightly burning sensation when incorporated in large quantities; and amino acids such as DL-alanine sometimes cause coloration or malodor.

Under these circumstances, the present inventors conducted intensive studies in order to obtain skin preparations for external use that had good storage stability, that exhibited a high moisture retaining effect and that were free from the problems of stickiness, coloration and malodor. As a result, the present inventors found that xylobiose-containing skin preparations for external use satisfied these requirements and the present invention has been accomplished on the basis of this finding.

The present invention is characterized by incorporation of xylobiose which results in solving the various problems encountered with the prior art skin preparations for external use.

Xylobiose used in the present invention is a disaccharide (mol. wt. 282) that, as shown below, comprises two molecules of xylose which is a pentose that are polymerized via β -1,4 bond:



Xylose is the constituent of xylan which is a polysaccharide in plants and it has long been taken into the human body as a non-calorie saccharide. Xylan is a kind of hemicelluloses that have recently come to be recognized as useful edible vegetable fibers and it is known that xylan occurs extensively in the fibrous portions of cottonseeds, corns, malt and sugar canes.

Xylobiose as it occurs naturally is known to be contained in bamboo in very small amount and in a free state.

Plant-derived fibers such as celluloses and hemicelluloses are used as starting materials for the manufacture of foods and cosmetics. Noting oligosaccharides which are fibrous polysaccharides of shorter sugar chains, the present inventors previously developed efficient processes for preparing xylobiose which occurs naturally in only very small amounts (Japanese Laid-Open Patent Application Nos. 155095/1987, 242592/1986 and 100694/1990).

As a result of continued studies, the present inventors have found that xylobiose is useful as a component of skin preparations for external use and that it provides preparations with the ability to retain moisture without causing any stickiness and that it is stable without causing coloration or malodor.

The skin preparations for external use that can benefit from the incorporation of xylobiose in accordance with the present invention include cosmetics, drugs, quasidugs and other products that are to be used on or applied to the skin or hair. Such skin preparations can be formulated in widely varying dosage forms including aqueous solutions, solubilizable systems, emulsions and water/oil bilayer systems. Specific examples of the skin preparations include cosmetics such as moisture creams, clear lotions, milky lotions, packs and lip treatments, drugs or quasidugs such as ointments and cataplasms, hair-care products such as hair treatments, rinses and hair conditioners, and detergents such as hair shampoos and body shampoos.

The amount in which xylobiose is to be incorporated in the preparation of the present invention is determined by its efficacy and economy. Having no toxicity to humans, xylobiose can be incorporated in any amount without causing the toxicity problem. However, in consideration of the need to achieve the intended effect and of the fact that increasing the xylobiose content beyond a certain level will not contribute to any corresponding enhancement of the efficacy, xylobiose may usually be incorporated in an

amount of 0.0001 - 20 wt%, preferably 0.1 - 10 wt%, of the total amount of the skin preparation on a dry solids basis.

Xylobiose can be used in the present invention as a xylobiose composition that is prepared by saccharifying xylan with a xylobiose generating enzyme. The thus prepared xylobiose composition contains xylan saccharified products other than xylobiose such as xylose and xylotriose. These materials will in no way impair the moisture retaining capability of xylobiose but the xylobiose content of said composition is preferably at least 20% (all percentages that appear hereinafter are on a weight basis), more preferably at least 50%.

As a xylobiose generating enzyme, there can be employed a commercially available enzyme, for example, derived from Trichoderma viride, Aspergillus niger, Humicola lanuginosa, Chaetomium graeile, or Bacillus Pumilus.

The skin preparations for external use of the present invention may contain known components in ordinary amounts. The components that can be used in addition to xylobiose in the skin preparation of the present invention are described below with reference to cosmetics.

Bases that can be used in cosmetics as an example of the skin preparations of the present invention may be selected from a class of bases that are commonly incorporated as cosmetic components and include the following: animal and plant derived materials such as almond oil, avocado oil, olive oil, turtle oil, bees wax, squalene, lanolin and castor oil; mineral materials such as liquid paraffin, ceresin, paraffin wax, microcrystalline wax, vaseline, candelilla wax, carnauba wax and Japan wax; fatty acids such as palmitic acid and stearic acid; alcohols such as ethanol; higher alcohols such as cetanol, stearyl alcohol, lanolin alcohol, octyl dodecanol and polyvinyl alcohol; esters such as isopropyl myristate, butyl stearate, acetoglyceride, acetylated lanolin, glycerin monostearate, polyoxyethylene monooleate ester, polyethylene glycol monostearic acid ester, and ethyl monooléate; amines such as triethanolamine; ethers such as polyoxyethylene cetyl ether; and silicone oils.

Besides these bases, the following components can be used as required: surfactants such as Spans, Tweens, sugar esters and polyhydric alcoholic esters; mucilages such as acasia gum, tragacanth gum, karaya gum, quince gum, pectin, methyl cellulose, hydroxymethyl propyl cellulose and carboxymethyl cellulose sodium; humectants such as glycerin, propylene glycol, sorbitol, diethylene glycol monoethyl ether and citric acid; extracts from various animals and plants; vitamins; amino acids; activators such as agents to enhance blood circulation; various enzymes; antiinflammatories; saccharides; pigments; biocides or preservatives; antioxidants; and perfumes.

To evaluate safety for humans and animals, cosmetics incorporating xylobiose according to the present invention were subjected to tests on percutaneous acute toxicity and skin irritation and nothing abnormal was found on the skin.

An example of the process for preparing xylobiose that can be used in the skin preparation of the present invention is described below.

Reference Example (for the preparation of xylobiose)

A plant-derived xylan as a starting material was saccharified in an aqueous solution with a xylobiose generating enzyme at 40 °C for 19 h at a pH of 7.0. After filtration, the resulting saccharified solution was treated with activated carbon and concentrated sulfuric acid at 60 °C for 2 h at a pH of 2.0 to effect discoloration and deprotenization. Diatomaceous earth was added to the treated product and the mixture was filtered with a filter press. Subsequently, the filtrate was concentrated by reverse osmosis to obtain a concentrated saccharified solution. This solution was desalted by successive passage through a cation-exchange resin, an anion-exchange resin and a mixed-bed resin. Activated carbon was added to the treated solution, which was held at 25 °C for 30 min at a pH of 4 - 6.5 to effect discoloration. Diatomaceous earth was added to the obtained solution, which was then filtered with a filter press. The filtrate was concentrated under vacuum at 60 °C for 4 h to prepare a xylobiose composition.

The xylan saccharified product thus obtained contained xylobiose as the main ingredient, with xylose, xylotriose and other substances being present in only negligible amounts. The saccharified products concomitant to xylobiose are in no way detrimental to the moisture retaining capability of xylobiose but the content of xylobiose in the xylobiose composition is desirably at least 20%. If necessary, the concentration of xylobiose can be enhanced with the aid of a reverse osmotic membrane.

The xylobiose composition thus obtained was treated with a reverse osmotic membrane to increase the xylobiose content to at least 95%.

The following experimental examples and working examples are provided for the purpose of further illustrating the present invention.

Experimental Example 1: Measurement of moisture retaining capability of xylobiose in terms of the rate of water evaporation (on aqueous solutions)

Various humectants were dissolved in water to make 50% aqueous solutions and their hygroscopic property at high humidity as well as their ability to retain water at low humidity were evaluated.

- 5 Material under test: Xylobiose composition (containing at least 95% xylobiose)
- Comparative humectants: Sorbitol
 1,3-butylene glycol
 Propylene glycol
 Glycerin
- 10 Testing environment: Condition A ... 35°C and 95% r.h. (this condition was created in a
 thermostatic chamber at 35°C by leaving in it a desiccator that contained a
 saturated aqueous solution of sodium monohydrogen phosphate.)
 Condition B ... 35°C and 40% r.h. (this condition was created in a
 thermostatic chamber at 35°C by leaving in it a desiccator that contained a
 solution of calcium chloride.)
- 15 Method of measurement: Each of the material under test and the comparative humectants was
 dissolved in water to make a 50% aqueous solution; 2 g of the solution was
 left under either condition A or B for 24 h and 70 h to measure the
 resulting changes in weight.
- 20 Results of measurement:
- (1) High-humidity condition (A) Under the high-humidity condition, all
 samples absorbed water but in varying degrees: after 70 h, the material
 under test (xylobiose) experienced a weight change of +6.1% whereas
 the respective values for the comparative humectants were +27.6%
 25 (glycerin), +26.5% (propylene glycol), +19.8% (1,3-butylene glycol)
 and +10.9% (sorbitol). It was therefore clear that xylobiose was less
 prone to absorb moisture than the comparative humectants under high
 humidity (see Table 1).
- (2) Low-humidity condition (B) Under the low-humidity condition, all
 30 samples experienced evaporation but in varying degrees: after 70 h, the
 material under test (xylobiose) experienced a weight change of -42.4%
 whereas the respective values for the comparative humectants were
 -39.9% (glycerin), -45.7% (propylene glycol), -44.3% (1,3-butylene gly-
 35 col) and -42.5% (sorbitol). Obviously, xylobiose was less effective than
 glycerin in retaining moisture at low humidity but it was more effective
 than the other comparative humectants (see Table 2).
- Discussion : On the basis of the results described above, it can be concluded that under
 high-humidity conditions such as in summer, xylobiose absorbs less mois-
 ture and hence is less sticky whereas under low-humidity conditions,
 40 xylobiose prevents evaporation of water from the skin. Hence, xylobiose
 has ideal properties as a humectant to be incorporated in cosmetics.
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- 55

Table 1

Weight changes at 95% r.h. and 35°C

Test material	Weight, g (parenthesized figures refer to percent weight change)		
	0 h	24 h	70 h
Xylobiose composition	2.00	2.01486(0.743)	2.12140(6.07)
Sorbitol	2.00	2.06613(3.31)	2.21764(10.88)
1,3-Butylene glycol	2.00	2.12273(6.14)	2.39539(19.77)
Propylene glycol	2.00	2.18533(9.27)	2.53065(26.53)
Glycerin	2.00	2.19537(9.77)	2.55151(27.58)

Table 2

Weight changes at 40% r.h. and 35°C

Test material	Weight, g (parenthesized figures refer to percent weight change)		
	0 h	24 h	70 h
Xylobiose composition	2.00	1.31634(-34.18)	1.15121(-42.44)
Sorbitol	2.00	1.42623(-28.69)	1.14923(-42.54)
1,3-Butylene glycol	2.00	1.49765(-25.12)	1.11389(-44.31)
Propylene glycol	2.00	1.61146(-19.43)	1.08590(-45.71)
Glycerin	2.00	1.64412(-17.79)	1.20282(-39.86)

Experimental Example 2: Measurement of moisture retaining capability in terms of the rate of water evaporation (on moisture creams)

Material under test: Xylobiose composition (containing at least 95% xylobiose)

Comparative humectants: Sorbitol
1,3-butylene glycol
Propylene glycol
Glycerin

Testing environment: Condition A ... 25°C and 38% r.h. (this condition was created in a thermostatic chamber at 25°C by leaving in it a desiccator that contained a solution of calcium chloride.)
Condition B ... 35°C and 40% r.h. (this condition was created in a thermostatic chamber at 35°C by leaving in it a desiccator that contained a

Moisture cream: solution of calcium chloride.)
 Commercial product
 Method of measurement: To each of the moisture creams provided, the material under test or the comparative humectants were added, each one in an amount of 5%, the creams were then left to stand under condition A or B and their weight was measured at 24, 48 and 72 h to determine the changes from the 0-h value. As a control, an O/W cream containing no humectant was provided.

Results:

(1) Comparison between O/W cream containing the material under test and the control The weight change that occurred in the O/W cream containing the material under test was -3.6% under condition A and -16.8% under condition B after 72 h. In comparison, the control cream experienced weight changes of -13.1% and -31.8% under conditions A and B, respectively. It was therefore apparent that the moisture retention of cream was enhanced by addition of the material under test (see Tables 3 and 4).

(2) Comparison between the material under test and the comparative humectants

After 72 h standing under condition A, the O/W cream containing the material under test experienced a weight change of -3.6%, which indicates the better moisture retaining quality of xylobiose than 1,3-butyleneglycol (-3.6%), glycerin (-3.8%), propyleneglycol (-3.9%) and sorbitol (-3.9%) (see Table 3). Similar results were obtained after standing for 24 h and 48 h.

After 72 h standing under condition B, the O/W cream containing the material under test experienced a weight change of -16.8%, which indicates the better moisture retaining quality of xylobiose than 1,3-butyleneglycol (-16.9%), glycerin (-17.4%), propyleneglycol (-18.6%) and sorbitol (-17.9%) (see Table 4).

Table 3

Weight changes at 38% r.h. and 25°C

Test material	Cream weight (g)	Total weight (container + cream) g, (parenthesized figures refer to percent weight change)			
		0 h	24 h	48 h	72 h
Xylobiose composition	10.41	16.8051	16.5923(-2.04)	16.5121(-2.81)	16.4323(-3.58)
Sorbitol	10.04	16.4089	16.1593(-2.49)	16.0846(-3.23)	16.0146(-3.93)
1,3-Butylene glycol	10.04	16.3207	16.0881(-2.32)	16.0193(-3.00)	15.9558(-3.63)
Propylene glycol	9.96	16.3260	16.0824(-2.45)	16.0040(-3.23)	15.9430(-3.85)
Glycerin	10.60	16.9012	16.6313(-2.55)	16.5574(-3.24)	16.5020(-3.77)
Control (no humectant added)	7.10	11.1514	10.8811(-3.81)	10.4824(-9.42)	10.2237(-13.07)

Table 4

Weight changes at 40% r.h. and 35°C

Test material	Cream weight (g)	Total weight (container + cream) g, (parenthesized figures refer to percent weight change)			
		0 h	24 h	48 h	72 h
Xylobiose composition	10.24	16.6145	15.8604(-7.36)	15.3467(-12.38)	14.8967(-16.78)
Sorbitol	10.33	16.7210	16.0532(-6.46)	15.5193(-11.63)	14.8703(-17.92)
1,3-Butylene glycol	10.24	16.4862	15.8411(-6.30)	15.3356(-11.24)	14.7528(-16.93)
Propylene glycol	9.86	16.3127	15.5515(-7.72)	14.9856(-13.46)	14.4817(-18.57)
Glycerin	10.26	16.5508	15.8313(-7.01)	15.3524(-11.68)	14.7690(-17.37)
Control (no humectant added)	5.88	9.8746	8.9057(-16.48)	8.3494(-25.94)	8.0032(-31.83)

Discussion : On the basis of the results described above, it can be concluded that the O/W cream containing xylobiose is comparable to or more effective than the O/W creams containing other humectants as regards moisture retention.

The moisture cream containing xylobiose that was prepared in Experimental Example 2 was actually applied to the skin; it had high affinity for the skin, produced a refreshing feel, had no stickiness, and hence was found to be satisfactory from an organoleptic viewpoint.

The following working examples are provided for describing the formulations of various products in

accordance with the present invention and the processes for producing them.

Example 1: Clear lotion

5 A xylobiose-containing clear lotion was prepared to the recipe described below:

	<u>Component</u>	<u>Amount (%)</u>
10	Xylobiose composition (containing at least 95% xylobiose)	1.0
	Propylene glycol	1.0
	Citric acid	0.2
15	95% Ethanol	10.0
	Perfume	q.s.
20	POE lauryl ether	0.5
	Distilled water	bal.

When actually applied to the skin, the lotion had good affinity for the skin, produced a refreshing feel,
25 had no stickiness and hence was found to be satisfactory from an organoleptic viewpoint.

Example 2: Milky lotion

30 A xylobiose-containing milky lotion was prepared to the recipe described below. When actually applied
to the skin, the lotion had good affinity for the skin, produced a refreshing feel, had no stickiness and hence
was found to be satisfactory from an organoleptic viewpoint.

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	<u>Component</u>	<u>Amount (%)</u>
	Oily ingredients: stearic acid	2.0
5	cetanol	1.5
	Vaseline	3.0
	lanolin alcohol	2.0
10	liquid paraffin	10.0
	Emulsifier : polyoxyethylene monooleic acid ester	2.0
15	Perfume	0.5
	Antiseptic and antioxidant	q.s.
20	Humectant : xylobiose composition (containing at least 95% xylobiose)	8.0
	Alkali : triethanolamine	1.0
25	Purified water	70.0

30 Example 3: Nourishing cream

A xylobiose-containing nourishing cream was prepared to the recipe described below. When actually applied to the skin, the cream had good affinity for the skin, produced a refreshing feel, had no stickiness and hence was found to be satisfactory from an organoleptic viewpoint.

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	<u>Component</u>	<u>Amount (%)</u>
	Stearic acid	2.0
40	Stearyl alcohol	7.0
	Reduced lanolin	2.0
	Squalane	5.0
45	Octyl dodecanol	6.0
	POE (25 mol%) cetyl ether	3.0
50	Glycerin monostearate	2.0
	Antiseptic	q.s.
	Perfume	q.s.
55	Propylene glycol	5.0

Xylobiose composition (containing
at least 95% xylobiose) 1.0

Distilled water bal.

Example 4: Pack

A xylobiose-containing pack was prepared to the recipe described below. When actually applied to the skin, the pack had good affinity for the skin, produced a refreshing feel, had no stickiness and hence was found to be satisfactory from an organoleptic viewpoint.

	<u>Component</u>	<u>Amount (%)</u>
15	Film forming agent: polyvinyl alcohol	15.0
	Thickener: sodium carboxymethyl cellulone	5.0
20	Humectant: xylobiose-containing composition (containing at least 95% xylobiose)	3.0
	Ethanol	10.0
25	Perfume	0.5
	Antiseptic and antioxidant	q.s.
30	Purified water	66.5

Example 5: Lip treatment

A xylobiose-containing lip treatment was prepared to the recipe described below. When actually applied to the skin, the treatment had good affinity for the skin, produced a refreshing feel, had no stickiness and hence was found to be satisfactory from an organoleptic viewpoint.

	<u>Component</u>	<u>Amount (%)</u>
40	Candelilla wax	9.0
	Solid paraffin	8.0
45	Beeswax	5.0
	Carnauba wax	5.0
50	Lanolin	11.0
	Castor oil	bal.
55	Xylobiose-containing composition (containing at least 95% xylobiose)	0.1
	Isopropyl myristate	10.0

Perfume q.s.
 Antioxidant q.s.

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Example 6: Ointment

10 A xylobiose-containing ointment was prepared to the recipe described below. When actually applied to the skin, ointment had good affinity for the skin, produced a refreshing feel, had no stickiness and hence was found to be satisfactory from an organoleptic viewpoint.

15	<u>Component</u>	<u>Amount (%)</u>
	Stearyl alcohol	18.0
	Japan wax	20.0
20	Xylobiose composition (containing at least 95% xylobiose)	0.5
	Ethyl monooleate	0.5
25	Vaseline	40.0
	Purified water	bal.

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Example 7: Hair shampoo

A xylobiose-containing hair shampoo was prepared to the recipe described below. When actually applied to the hair, a natural oiliness was imparted both to the skin and hair and the results were
 35 satisfactory from an organoleptic viewpoint.

	<u>Component</u>	<u>Amount (%)</u>
40	Hydroxymethylpropyl cellulose	0.2
	Water	56.0
	Amisoft CT-12 (30% aq. sol.)	29.0
45	Amizol CDE	4.5
	Sodium salt	0.4
50	Xylobiose composition (containing at least 95% xylobiose)	8.9
	Polyethylene glycol monostearate	1.0

55 As is clear from the foregoing description, the skin preparations for external use that incorporate xylobiose in accordance with the present invention are free from the problems of stickiness, color change and malodor and prove very effective in moisture retention and in reducing excessive roughness and dryness of the skin and hair.

Claims

1. A skin preparation for external use that contains xylobiose.
- 5 2. A skin preparation according to claim 1 wherein xylobiose is contained in an amount of 0.0001 - 20 wt% of the total amount of the preparation.
3. A skin preparation according to claim 2 wherein xylobiose is contained in an amount of 0.1 - 10 wt%.
- 10 4. A skin preparation according to claim 1 which is a drug, a quasidrug, a cosmetic, a hair-care product or a detergent.

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EUROPEAN SEARCH REPORT

Application Number

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	PATENT ABSTRACTS OF JAPAN, vol. 13, no. 595 (C-672)[3943], 27th December 1989; & JP-A-1 252 281 (NAKANO VINEGAR CO., LTD) 06-10-1989 * Abstract * -----	1,4	A 61 K 7/06 A 61 K 7/48
X	WPIL, FILE SUPPLIER, AN = 89-337029, Derwent Publications Ltd, London, GB; & JP-A-1 252 280 (NAKANO SUMISE K.K.) 06-10-1989 * Abstract * -----	1,4	
X	PATENT ABSTRACTS OF JAPAN, vol. 9, no. 188 (C-295)[1911], 3rd August 1985; & JP-A-60 58 070 (RIKAGAKU KENKYUSHO) 04-04-1985 * Abstract * -----	1,4	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 K
Place of search		Date of completion of search	Examiner
The Hague		13 August 91	SIERRA GONZALEZ M.T.
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			